



P.B.5818 - Patentlaan 2  
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Europäisches  
Patentamt

Zweigstelle  
in Den Haag  
Recherchen-  
abteilung

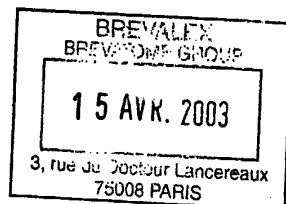
European  
Patent Office

Branch at  
The Hague  
Search  
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Office européen  
des brevets

Département à  
La Haye  
Division de la  
recherche

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Datum/Date

14. 04. 03

ichen/Ref./Réf.

SR 21180 US/EE

Anmeldung Nr./Application No./Demande n°/Patent Nr./Patent No./Brevet n°.  
00961335.7

imelder/Applicant/Demandeur/Patentinhaber/Proprietor/Titulaire  
Canfield, William M.

## COMMUNICATION

The European Patent Office herewith transmits

- ☐ the European search report
- ☐ the declaration under Rule 45 EPC
- ☐ the partial European search report under Rule 45 EPC
- ☒ the supplementary European search report concerning the international application under Article 157(2) EPC relating to the above-mentioned European patent application. Copies of the documents cited in the search report are enclosed.

The following specifications given by the applicant have been approved by the Search Division :

- ☐ Abstract
  - ☐ Title
  - ☐ Figure
  - ☐ The abstract was modified by the Search Division and the definitive text is attached to this communication.
  - ☐ The following figure will be published with the abstract, since the Search Division considers that it better characterises the invention than the one indicated by the applicant.
- Figure:
- ☒ Additional copy(copies) of the documents cited in the European search report.

## REFUND OF THE SEARCH FEE

If applicable under Article 10 Rules relating to fees, a separate communication from the Receiving Section on the refund of the search fee will be sent later.



EPO Form 1507 02.93




### CLAIMS INCURRING FEES

The present European patent application comprised at the time of filing more than ten claims.

- ☐ Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims and for those claims for which claims fees have been paid, namely claim(s):
- ☐ No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims.

### LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

- ☐ All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.
- ☐ As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.
- ☒ Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:  
1-67, 74-105
- ☐ None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:



Although claims 74-81 are directed to a method of treatment of the human/animal body (Article 52(4) EPC), the search has been carried out and based on the alleged effects of the compound/composition.

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Claim(s) searched incompletely:  
43, 49, 52, 57, 67, 69, 76, 79, 80

Reason for the limitation of the search:

Present claims 43, 52, 67, 69, 76, 79 and 80 and especially Claims 49 and 57 relate to an extremely large number of possible compounds or methods. Support within the meaning of Article 84 EPC and/or disclosure within the meaning of Article 83 EPC is to be found, however, for only a very small proportion of the compounds or methods claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Unless the alternatives in said claims 43, 52, 67, 69, 76, 79 and 80 relate to a claim which itself is novel and inventive, they will give rise to further non-unity objections. The same applies for claims 49 and 57 provided an attempt will be made to specify the compounds claimed. In this context it should be emphasised that the drafting of the claims lies exclusively in the responsibility of the Applicant and that e.g. non-unity objections which arise due to the drafting of certain subject-matter in an independent form, cannot be cured by making reference to the fact that said independently claimed subject-matter forms part of a common (but unfortunately known) concept, e.g. two independently claimed steps of a known process.



The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. Claims: 1-18, 82, 84, 86, 88-105

GlcNAc-phosphotransferase and subunits thereof, an antibody binding it, nucleotide sequences encoding it or encoding the subunits, methods for producing the enzyme, vectors and host cell comprising the nucleotide sequences coding for the enzyme or the subunits

2. Claims: 19-34, 83, 85, 87

Phosphodiester alpha-GlcNAcase, an antibody binding it, nucleotide sequence encoding it, vectors and host cells comprising the nucleotide sequence and methods for producing the enzyme

3. Claims: 35-48

Method of modifying lysosomal hydrolases comprising contacting said lysosomal hydrolases with an isolated GlcNAc-phosphotransferase

4. Claims: 49-67

Phosphorylated lysosomal hydrolase comprising a mannose 6-phosphate and methods for preparing phosphorylated lysosomal hydrolase

5. Claims: 68-73

High mannose lysosomal hydrolase and methods for producing it

6. Claims: 74-81

Methods of treating a patient suffering from a lysosomal storage disease



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# SUPPLEMENTARY

## PARTIAL EUROPEAN SEARCH REPORT

Application Number

which under Rule 45 of the European Patent Convention shall be considered, for the purposes of subsequent proceedings, as the European search report

EP 00 96 1335

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
X	ZHAO K-W ET AL: "PURIFICATION AND CHARACTERIZATION OF HUMAN LYMPHOBLAST N ACETYLGLUCOSAMINE-1-PHOSPHOTRANSFERASE" GLYCOBIOLOGY, vol. 2, no. 2, 1992, pages 119-125, XP009003096 ISSN: 0959-6658 see the whole document	1,2	C12N9/12 C12N9/14 C12N1/20 C12N15/00 C07H21/04 A61K38/44 A61K38/51 C07K14/00
Y	---	35-48	
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The supplementary search report has been based on the last set of claims valid and available at the start of the search.			TECHNICAL FIELDS SEARCHED (Int.Cl.7)
INCOMPLETE SEARCH			C12N
The Search Division considers that the present application, or some or all of its claims, does/do not comply with the EPC to such an extent that a meaningful search into the state of the art cannot be carried out, or can only be carried out partially, for the following claims:  Claims searched completely :  Claims searched incompletely :  Claims not searched :  Reason for the limitation of the search:  see sheet C			
6	Place of search MUNICH	Date of completion of the search 26 March 2003	Examiner Grosskopf, R
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document			

EPO FORM 1503 03.02 (P04C20)



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SUPPLEMENTARY

PARTIAL EUROPEAN SEARCH REPORT

Application Number

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DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
P,X	NAGASE T ET AL: "PREDICTION OF THE CODING SEQUENCES OF UNIDENTIFIED HUMAN GENES. XV.THE COMPLETE SEQUENCE OF 100 NEW CDNA CLONES FROM BRAIN WHICH CODE FOR LARGE PROTEINS IN VIVO" DNA RESEARCH, UNIVERSAL ACADEMY PRESS, JP, vol. 6, no. 5, October 1999 (1999-10), pages 337-345, XP000865804 ISSN: 1340-2838 see the whole document	8-10, 88-99	
P,X	-& DATABASE SWALLPROT 'Online! 1 May 2000 (2000-05-01) retrieved from EBI Database accession no. Q9ULL2 XP002226188 * abstract * 99.8% identity with SEQ ID NO: 1 from aa 308-930 and 100% identity with SEQ ID NO: 2 ---	8-10, 88-99	
			TECHNICAL FIELDS SEARCHED (Int.Cl.7)
X	DATABASE SWALLPROT 'Online! 1 November 1996 (1996-11-01) retrieved from EBI Database accession no. Q61340 XP002226187 57.9% identity with SEQ ID NO: 1 in 285 aa overlap (aa 645-930 of SEQ ID NO: 1). ---	8-10,91	
X	WO 99 31117 A (FLORENCE KIMBERLY ;HUMAN GENOME SCIENCES INC (US); FENG PING (US);) 24 June 1999 (1999-06-24) Human secreted protein encoded by gene 6 has 100% identity with SEQ ID NO: 3 see SEQ ID NO: 130 --- -/--	8-10, 102-105	

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EPO FORM 1503 03.98 (P04C28)



**SUPPLEMENTARY**  
**PARTIAL EUROPEAN SEARCH REPORT**

Application Number

EP 00 96 1335

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SUPPLEMENTARY

PARTIAL EUROPEAN SEARCH REPORT

Application Number

EP 00 96 1335

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
Y	BARANSKI THOMAS J ET AL: "Lysosomal enzyme phosphorylation: I. Protein recognition determinants in both lobes of procathepsin D mediate its interaction with UDP-GlcNAc:Lysosomal enzyme N-acetylglucosamine-1-phosphotransferase." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 267, no. 32, 1992, pages 23342-23348, XP002235769 ISSN: 0021-9258 see the whole document ---	35-48	
Y	TIKKANEN RITVA ET AL: "Several cooperating binding sites mediate the interaction of a lysosomal enzyme with phosphotransferase." EMBO (EUROPEAN MOLECULAR BIOLOGY ORGANIZATION) JOURNAL, vol. 16, no. 22, 17 November 1997 (1997-11-17), pages 6684-6693, XP002235770 ISSN: 0261-4189 see the whole document ---	35-48	TECHNICAL FIELDS SEARCHED (Int.Cl.7)
X	MATSUURA ET AL: "Human alpha-galactosidase A: characterization of the N-linked oligosaccharides on the intracellular and secreted glycoforms overexpressed by Chinese hamster ovary cells" GLYCOBIOLOGY, IRL PRESS,, GB, vol. 8, no. 4, April 1998 (1998-04), pages 329-339, XP000925912 ISSN: 0959-6658 see abstract --- -/--	49,57	





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Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
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X	BARTON N W ET AL: "THERAPEUTIC RESPONSE TO INTRAVENOUS INFUSIONS OF GLUCOCEREBROSIDASE IN A PATIENT WITH GAUCHER DISEASE" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 87, March 1990 (1990-03), pages 1913-1916, XP002905934 ISSN: 0027-8424 see the whole document ---	74-81	TECHNICAL FIELDS SEARCHED (Int.Cl.7)
X	BRADY R O ET AL: "Modifying Exogenous Glucocerebrosidase for Effective Replacement Therapy in Gaucher Disease." JOURNAL OF INHERITED METABOLIC DISEASE, vol. 17, no. 4, 1994, pages 510-519, XP009008428 ISSN: 0141-8955 see the whole document, esp. Fig. 4 --- -/--	74-81	



DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
Y	KAKKIS E D ET AL: "OVEREXPRESSION OF THE HUMAN LYSOSOMAL ENZYME ALPHA-L-IDURONIDASE IN CHINESE HAMSTER OVARY CELLS" PROTEIN EXPRESSION AND PURIFICATION, ACADEMIC PRESS, US, vol. 5, no. 3, June 1994 (1994-06), pages 225-232, XP000857380 ISSN: 1046-5928 see the whole document ---	74-81	
Y	ZHAO KE-WEI ET AL: "Carbohydrate structures of recombinant human alpha-L-iduronidase secreted by Chinese hamster ovary cells." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 272, no. 36, 1997, pages 22758-22765, XP002235771 ISSN: 0021-9258 see the whole document ---	74-81	TECHNICAL FIELDS SEARCHED (Int.Cl.7)
Y	ZIEGLER R J ET AL: "CORRECTION OF ENZYMATIC AND LYSOSOMAL STORAGE DEFECTS IN FABRY MICE BY ADENOVIRUS-MEDIATED GENE TRANSFER" HUMAN GENE THERAPY, XX, XX, vol. 10, no. 10, 1 July 1999 (1999-07-01), pages 1667-1682, XP001012918 ISSN: 1043-0342 see the whole document ---- -/--	74-81	



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Y	SUN HUAICHANG ET AL: "Retrovirus vector-mediated correction and cross-correction of lysosomal alpha-mannosidase deficiency in human and feline fibroblasts." HUMAN GENE THERAPY, vol. 10, no. 8, 20 May 1999 (1999-05-20), pages 1311-1319, XP009008322 ISSN: 1043-0342 see the whole document	74-81	
Y	REUSER A J J ET AL: "Lysosomal storage diseases: Cellular pathology, clinical and genetic heterogeneity, therapy." ANNALES DE BIOLOGIE CLINIQUE, vol. 52, no. 10, 1994, pages 721-728, XP009008339 ISSN: 0003-3898 see pages 726-727 "Therapy"	74-81	TECHNICAL FIELDS SEARCHED (Int.Cl.7)

**ANNEX TO THE EUROPEAN SEARCH REPORT  
ON EUROPEAN PATENT APPLICATION NO.**

EP 00 96 1335

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.  
The members are as contained in the European Patent Office EDP file on  
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26-03-2003

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